REMARKS

Status of the Claims

Claims 1-3, 5-15, 17-23, 27-30, 33-35, 38, 40-43, 45, 47, 48, 50, 52, 53, 56-59, 61-64, 66-71, 83-88, 90, 93, 94 and 97-101 are currently pending and under examination. Claims 15, 17, 19-21, 23, 27, 28, 48, 50, 53, 57, 85-87, 93, 97, 100 and 101 stand withdrawn from consideration as being directed to a nonelected invention. Claims 27, 28, 84 and 94 are canceled herein without prejudice. Claims 1, 34, 59, 69, 70 and 85-88 are amended herein. The claim amendments are supported by the specification at, e.g., page 21, lines 27-29, page 22, lines 5-8, page 26, lines 7-11, and by the claims as filed, or are editorial in nature. No new matter is added by way of these amendments. Entry of the claim amendments and reconsideration in view of the following remarks are respectfully requested.

Formal Matters

Applicants thank the Examiner for modifying the "restriction" requirement to be treated as a species election.

Claim Objections under 37 C.F.R. § 1.75(c)

Claims 85-88 are objected to under 37 C.F.R. § 1. 75 (c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicants respectfully traverse the objection.

Claims 85-87 are rewritten herein in independent form, rendering the objections moot with respect to these claims. Claim 88 is already presented in independent form. In view of the foregoing, Applicants respectfully request that the claim objections be withdrawn.

Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 1-3, 5-14, 18, 22, 29, 30, 33-35, 38, 40-43, 45, 47, 52, 56, 58, 59, 61-64, 66-71, 83, 84, 88, 90, 94, 98, and 99 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly

being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants respectfully traverse the rejections.

"The definiteness inquiry focuses on whether those skilled in the art would understand the scope of the claim when the claim is read in light of the rest of the specification." *Union Pacific Resources Co.* v. *Chesapeake Energy Corp.*, 236 F.3d 684,692 (Fed. Cir. 2001).

With regard to claims 1, 34, and 88, the Examiner has taken the position that the reference to a "cell stimulatory polypeptide" renders the claims indefinite because it allegedly fails to set forth any meaningful structural/functional characteristics of the claim polypeptide. Solely to advance prosecution, claims 1 is amended herein to include limitations from claim 7, and claim 7 is canceled herein without prejudice. Additional support is provided by the specification at, e.g., page 26, lines 7-11. Similar limitations are incorporated into claims 34 and 88. Applicants submit that one of ordinary skill in the art would readily understand the allegedly indefinite phrase.

In addition, the phrases "at least about 75%", "about seven to ten days", and "about 14 days" are said to be vague and indefinite parameters for which the metes and bounds of the invention cannot be ascertained. Applicants respectfully disagree, and submit that one of skill in the art would reasonably understand the intended metes and bounds of the claims. Nevertheless, to facilitate prosecution, the phrase "at least about" is amended to recite "at least" for clarity. Applicants respectfully submit that the phrases "about seven to ten days" and "about 14 days" are sufficiently clear to one of skill in the art when read in light of the specification as a whole.

Claim 34 is amended to correct a typographical error. Specifically, the recitation of "and/or" in the preamble is deleted. Claim 59 is amended to delete the recitation of a "cell surface binding stimulatory peptide" which, as noted by the Examiner, is already included in claim 34.

Claim 70 is amended as suggested by the Examiner to clarify that the cells in step (a) of method 34 are isolated from an individual infected with HIV. Applicants thank the Examiner for the helpful suggestion.

Claims 84 and 94 are canceled herein without prejudice, rendering the indefiniteness rejections of these claims moot.

In view of the foregoing remarks, Applicants respectfully submit that the claims are clear and definite. Applicants request that the rejections under 35 U.S.C. § 112, second paragraph, be withdrawn.

Rejections under 35 U.S.C. § 112, First Paragraph

Claims 1-3, 5-14, 18, 22, 29, 30, 33, 34, 35, 38, 40-43, 45, 47, 52, 56, 58, 59, 61-64, 66-71, 83, 84, 88, 90, 94, 98, and 99 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner asserts that the specification fails to provide adequate support for the genus of cell surface binding molecules and cell types transduced with said molecules and a lentiviral vector. Applicants respectfully traverse the rejections for at least the following reasons.

As discussed above, claims 1 and 34 are amended herein solely to facilitate prosecution. As amended, claims 1 and 34 recite that the "cell stimulatory polypeptide" is an antibody, an antigen binding fragment, or a ligand. Support is provided by the specification at, e.g., page 26, lines 7-11. Further, the claims relate to methods for transducing primary lymphoid, myeloid and hematopoietic progenitor cells. Support for the claimed cell types is provided by the specification at, e.g., page 8, lines 7 and 14-16. Applicants respectfully submit that these elements of the claims cannot be considered in isolation of one another, as a person of skill in the art would clearly understand that the claimed cell type will necessarily define, and at least inherently determine, the cell stimulatory polypeptides useful for the particular cell type(s).

With regard to specific assertions on page 7 of the Office Action, the Applicants respectfully note that claim 1 does not recite a "polypeptide which binds with said cell surfaces by binding to a T cell surface receptor"; and claim 34 does not recite "at least one polypeptide that physically interacts with a receptor on the surface of the primary T cell or T stem cell." The Examiner has further asserted that specification fails to provide adequate guidance pertaining to the

T-cell surface receptor of interest. Applicants respectfully note that this is not a limitation that appears in the present claims, and requests further clarification from the Examiner.

Rejections under 35 U.S.C. §103(a)

Claims 1-3, 5-4, 18, 22, 29, 30, 33, 34, 35, 38, 40-43, 45, 47, 52, 56, 58, 59, 61-64, 66-69, 78, 83, 88, 90, 98 and 99 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Costello et al. (2000) in view of Quinn et al. (1998). Applicants traverse the rejections for the following reasons.

To establish a *prima facie* case of obviousness, the Office must provide one or more references that, *inter alia*, teach or suggest all the limitations of the claimed invention. While the strict teaching - suggestion - motivation (TSM) test was rejected by the Supreme Court in *KSR v. Teleflex*, there still must be an "articulated reasoning with some rational underpinning to support the legal conclusion" of obviousness. *KSR International Co. v. Teleflex, Inc.*, 82 U.S.P.Q.2d 1385, at 1396 (S. Ct. 2007). Determining if there is an articulated reason requires analysis of a number of factors, including, e.g., whether there is evidence of teaching away and whether there is a reasonable expectation of success. In order for a combination of documents to defeat patentability, the Court in *KSR* held that the practitioner must have some reason to combine the elements in the way the claimed new invention does.

The alleged teachings of Costello et al. are described on pages 13-15 of the Office Action. The Examiner acknowledges that Costello et al. do not disclose a transduction efficiency of ~75% after 14 days.

The alleged teaching of Quinn et al. are set forth on pages 12-13 of the Office Action. The Examiner acknowledges that Quinn et al. did not employ a lentiviral-based vector. However, the Examiner takes the position that it would have been *prima facie* obvious to one of ordinary skill to employ different multiplicities of infection in the assay of Costello et *al.* (2000), since Quinn et al. (1998) teach that increasing MOIs correlate with increasing transduction efficiencies.

The claims, as amended, are directed towards methods of stably transducing primary lymphoid cells, myeloid cells or hematopoietic progenitor cells comprising contacting the cells with a lentiviral vector and a cell stimulatory polypeptide, which can be an antibody, an antigen binding fragment or a ligand, wherein at least 90% of the cells are stably transduced after about seven to ten days, or at about 14 days. As discussed in more detail below, neither Costello et al. nor Quinn et al., alone or in combination, teach or otherwise suggest that the stable transduction of such a high percentage of cells can be achieved.

As discussed in the specification, Costello et al. describe the transduction of stimulated and non-stimulated T cells using HIV-1 lentiviral vectors, but only report a maximum of 17-19% efficiency on transduction. Costello et al. also reported increased efficiency to no more than 36% in stimulated T cells by including HIV-1 accessory proteins. See specification at, e.g., page 2, lines 22-27. Nothing in Costello et al. would lead one of skill in the art to reasonably expect that a transduction efficiency of at least 90% could be achieved. This deficiency is not remedied by combination with the teachings of Quinn et al.

Quinn et al. describe evaluation of gene transfer and gene expression in human T-cells activated with anti-CD3 MAb plus IL-2, or co-stimulation with co-immobilized anti-CD3 and anti-CD28 MAbs, See Quinn et al. at Abstract. Quinn et al. disclose that their transduction frequencies varied between 10 and 75% and reflected the MOI. See Quinn et al., page 1465, col. 1, first full paragraph. Quinn et al. do not disclose or otherwise suggest that efficiencies of 90% can be achieved, even by varying the MOI. Moreover, Quinn et al. use the MFG retroviral vector as opposed to the lentiviral vectors of the present invention.

The Examiner appears to suggest that one of skill in the art would be motivated to combine the teachings of Quinn et al. that increasing MOIs correlate with increasing transduction efficiencies with the method of Costello et al. Applicants respectfully disagree.

First, one of skill in the art could not reasonably predict based on the retroviral vector of Quinn et al. that similar transduction efficiencies or effects on varying the MOI would be achieved using the lentiviral vectors of Costello et al. Moreover, the Applicants submit that even if

combined, one of skill in the art would not have had a reasonable expectation based on the teachings of Costello et al. and Quinn et al. that transductions efficiencies of at least 90% could be achieved at about 7-10 days or at about 14 days. Accordingly, one of skill in the art would have neither a motivation nor a reasonable expectation of successfully achieving the invention as claimed.

In view of the foregoing remarks, Applicants respectfully request that the rejections under 35 U.S.C. 103(a) be withdrawn.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding objection to and rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below. In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 397272000401. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

Electronic signature: /Brenda J. Wallach/
Brenda J. Wallach
Registration No.: 45,193
MORRISON & FOERSTER LLP
12531 High Bluff Drive, Suite 100 San Diego,
California 92130-2040
(858) 720-7961